



IFW16

## RAW SEQUENCE LISTING

DATE: 10/07/2004

PATENT APPLICATION: US/10/705,633A

TIME: 09:37:01

Input Set : A:\568.1D1.TXT

Output Set: N:\CRF4\10072004\J705633A.raw

4 <110> APPLICANT: Madison, Edwin L  
 6 <120> TITLE OF INVENTION: TISSUE TYPE PLASMINOGEN ACTIVATOR (t-PA)  
 7 VARIANTS: COMPOSITIONS AND METHODS OF USE  
 10 <130> FILE REFERENCE: TSRI 568.1D1  
 12 <140> CURRENT APPLICATION NUMBER: US 10/705,633A  
 13 <141> CURRENT FILING DATE: 2003-11-10  
 15 <150> PRIOR APPLICATION NUMBER: US 09/600,985  
 16 <151> PRIOR FILING DATE: 2000-11-13  
 18 <150> PRIOR APPLICATION NUMBER: PCT/US97/20226  
 19 <151> PRIOR FILING DATE: 1997-11-12  
 21 <150> PRIOR APPLICATION NUMBER: US 60/030,655  
 22 <151> PRIOR FILING DATE: 1996-11-12  
 24 <160> NUMBER OF SEQ ID NOS: 12  
 26 <170> SOFTWARE: FastSEQ for Windows Version 4.0  
 28 <210> SEQ ID NO: 1  
 29 <211> LENGTH: 527  
 30 <212> TYPE: PRT  
 31 <213> ORGANISM: Homo sapiens  
 33 <400> SEQUENCE: 1  
 34 Ser Tyr Gln Val Ile Cys Arg Asp Glu Lys Thr Gln Met Ile Tyr Gln  
 35 1 5 10 15  
 36 Gln His Gln Ser Trp Leu Arg Pro Val Leu Arg Ser Asn Arg Val Glu  
 37 20 25 30  
 38 Tyr Cys Trp Cys Asn Ser Gly Arg Ala Gln Cys His Ser Val Pro Val  
 39 35 40 45  
 40 Lys Ser Cys Ser Glu Pro Arg Cys Phe Asn Gly Gly Thr Cys Gln Gln  
 41 50 55 60  
 42 Ala Leu Tyr Phe Ser Asp Phe Val Cys Gln Cys Pro Glu Gly Phe Ala  
 43 65 70 75 80  
 44 Gly Lys Cys Cys Glu Ile Asp Thr Arg Ala Thr Cys Tyr Glu Asp Gln  
 45 85 90 95  
 46 Gly Ile Ser Tyr Arg Gly Thr Trp Ser Thr Ala Glu Ser Gly Ala Glu  
 47 100 105 110  
 48 Cys Thr Asn Trp Asn Ser Ser Ala Leu Ala Gln Lys Pro Tyr Ser Gly  
 49 115 120 125  
 50 Arg Arg Pro Asp Ala Ile Arg Leu Gly Leu Gly Asn His Asn Tyr Cys  
 51 130 135 140  
 52 Arg Asn Pro Asp Arg Asp Ser Lys Pro Trp Cys Tyr Val Phe Lys Ala  
 53 145 150 155 160  
 54 Gly Lys Tyr Ser Ser Glu Phe Cys Ser Thr Pro Ala Cys Ser Glu Gly  
 55 165 170 175  
 56 Asn Ser Asp Cys Tyr Phe Gly Asn Gly Ser Ala Tyr Arg Gly Thr His  
 57 180 185 190

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58 Ser Leu Thr Glu Ser Gly Ala Ser Cys Leu Pro Trp Asn Ser Met Ile
59      195      200      205
60 Leu Ile Gly Lys Val Tyr Thr Ala Gln Asn Pro Ser Ala Gln Ala Leu
61      210      215      220
62 Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Gly Asp Ala Lys
63 225      230      235      240
64 Pro Trp Cys His Val Leu Lys Asn Arg Arg Leu Thr Trp Glu Tyr Cys
65      245      250      255
66 Asp Val Pro Ser Cys Ser Thr Cys Gly Leu Arg Gln Tyr Ser Gln Pro
67      260      265      270
68 Gln Phe Glu Ile Lys Gly Gly Leu Phe Ala Asp Ile Ala Ser His Pro
69      275      280      285
70 Trp Gln Ala Ala Ile Phe Ala Lys His Arg Arg Ser Pro Gly Glu Arg
71      290      295      300
72 Phe Leu Cys Gly Gly Ile Leu Ile Ser Ser Cys Trp Ile Leu Ser Ala
73 305      310      315      320
74 Ala His Cys Phe Gln Glu Arg Phe Pro Pro His His Leu Thr Val Ile
75      325      330      335
76 Leu Gly Arg Thr Tyr Arg Val Val Pro Gly Glu Glu Glu Gln Lys Phe
77      340      345      350
78 Glu Val Glu Lys Tyr Ile Val His Lys Glu Phe Asp Asp Asp Thr Tyr
79      355      360      365
80 Asp Asn Asp Ile Ala Leu Leu Gln Leu Lys Ser Asp Ser Ser Arg Cys
81      370      375      380
82 Ala Gln Glu Ser Ser Val Val Arg Thr Val Cys Leu Pro Pro Ala Asp
83 385      390      395      400
84 Leu Gln Leu Pro Asp Trp Thr Glu Cys Glu Leu Ser Gly Tyr Gly Lys
85      405      410      415
86 Asp Glu Ala Leu Ser Pro Phe Tyr Ser Glu Arg Leu Lys Glu Ala His
87      420      425      430
88 Val Arg Leu Tyr Pro Ser Ser Arg Cys Thr Ser Gln His Leu Leu Asn
89      435      440      445
90 Arg Thr Val Thr Asp Asn Met Leu Cys Ala Gly Asp Thr Arg Ser Gly
91      450      455      460
92 Gly Pro Gln Ala Asn Leu His Asp Ala Cys Gln Gly Asp Ser Gly Gly
93 465      470      475      480
94 Pro Leu Val Cys Leu Asn Asp Gly Arg Met Thr Leu Val Gly Ile Ile
95      485      490      495
96 Ser Trp Gly Leu Gly Cys Gly Gln Lys Asp Val Pro Gly Val Tyr Thr
97      500      505      510
98 Lys Val Thr Asn Tyr Leu Asp Trp Ile Arg Asp Asn Met Arg Pro
99      515      520      525
102 <210> SEQ ID NO: 2
103 <211> LENGTH: 527
104 <212> TYPE: PRT
105 <213> ORGANISM: Homo sapiens
107 <400> SEQUENCE: 2
108 Ser Tyr Gln Val Ile Cys Arg Asp Glu Lys Thr Gln Met Ile Tyr Gln
109 1      5      10      15

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```

110 Gln His Gln Ser Trp Leu Arg Pro Val Leu Arg Ser Asn Arg Val Glu
111          20          25          30
112 Tyr Cys Trp Cys Asn Ser Gly Arg Ala Gln Cys His Ser Val Pro Val
113          35          40          45
114 Lys Ser Cys Ser Glu Pro Arg Cys Phe Asn Gly Gly Thr Cys Gln Gln
115          50          55          60
116 Ala Leu Tyr Phe Ser Asp Phe Val Cys Gln Cys Pro Glu Gly Phe Ala
117 65          70          75          80
118 Gly Lys Cys Cys Glu Ile Asp Thr Arg Ala Thr Cys Tyr Glu Asp Gln
119          85          90          95
120 Gly Ile Ser Tyr Arg Gly Thr Trp Ser Thr Ala Glu Ser Gly Ala Glu
121          100         105         110
122 Cys Thr Asn Trp Asn Ser Ser Ala Leu Ala Gln Lys Pro Tyr Ser Gly
123          115         120         125
124 Arg Arg Pro Asp Ala Ile Arg Leu Gly Leu Gly Asn His Asn Tyr Cys
125          130         135         140
126 Arg Asn Pro Asp Arg Asp Ser Lys Pro Trp Cys Tyr Val Phe Lys Ala
127 145         150         155         160
128 Gly Lys Tyr Ser Ser Glu Phe Cys Ser Thr Pro Ala Cys Ser Glu Gly
129          165         170         175
130 Asn Ser Asp Cys Tyr Phe Gly Asn Gly Ser Ala Tyr Arg Gly Thr His
131          180         185         190
132 Ser Leu Thr Glu Ser Gly Ala Ser Cys Leu Pro Trp Asn Ser Met Ile
133          195         200         205
134 Leu Ile Gly Lys Val Tyr Thr Ala Gln Asn Pro Ser Ala Gln Ala Leu
135          210         215         220
136 Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Gly Asp Ala Lys
137 225         230         235         240
138 Pro Trp Cys His Val Leu Lys Asn Arg Arg Leu Thr Trp Glu Tyr Cys
139          245         250         255
140 Asp Val Pro Ser Cys Ser Thr Cys Gly Leu Arg Gln Tyr Ser Gln Pro
141          260         265         270
142 Gln Phe Glu Ile Lys Gly Gly Leu Phe Ala Asp Ile Ala Ser His Pro
143          275         280         285
144 Trp Gln Ala Ala Ile Phe Ala Lys His Arg Arg Ser Pro Gly Glu Arg
145          290         295         300
146 Phe Leu Cys Gly Gly Ile Leu Ile Ser Ser Cys Trp Ile Leu Ser Ala
147 305         310         315         320
148 Ala His Cys Phe Gln Glu Arg Phe Pro Pro His His Leu Thr Val Ile
149          325         330         335
150 Leu Gly Arg Thr Tyr Arg Val Val Pro Gly Glu Glu Glu Gln Lys Phe
151          340         345         350
152 Glu Val Glu Lys Tyr Ile Val His Lys Glu Phe Asp Asp Asp Thr Tyr
153          355         360         365
154 Asp Asn Asp Ile Ala Leu Leu Gln Leu Lys Ser Asp Ser Ser Arg Cys
155          370         375         380
156 Ala Gln Glu Ser Ser Val Val Arg Thr Val Cys Leu Pro Pro Ala Asp
157 385         390         395         400
158 Leu Gln Leu Pro Asp Trp Thr Glu Cys Glu Leu Ser Gly Tyr Gly Lys

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159          405          410          415
160 Glu Glu Ala Leu Ser Pro Phe Tyr Ser Glu Arg Leu Lys Glu Ala His
161          420          425          430
162 Val Arg Leu Tyr Pro Ser Ser Arg Cys Thr Ser Gln His Leu Leu Asn
163          435          440          445
164 Arg Thr Val Thr Asp Asn Met Leu Cys Ala Gly Asp Thr Arg Ser Gly
165          450          455          460
166 Gly Pro Gln Ala Asn Leu His Asp Ala Cys Gln Gly Asp Ser Gly Gly
167 465          470          475          480
168 Pro Leu Val Cys Leu Asn Asp Gly Arg Met Thr Leu Val Gly Ile Ile
169          485          490          495
170 Ser Trp Gly Leu Gly Cys Gly Gln Lys Asp Val Pro Gly Val Tyr Thr
171          500          505          510
172 Lys Val Thr Asn Tyr Leu Asp Trp Ile Arg Asp Asn Met Arg Pro
173          515          520          525
176 <210> SEQ ID NO: 3
177 <211> LENGTH: 527
178 <212> TYPE: PRT
179 <213> ORGANISM: Homo sapiens
181 <400> SEQUENCE: 3
182 Ser Tyr Gln Val Ile Cys Arg Asp Glu Lys Thr Gln Met Ile Tyr Gln
183 1          5          10          15
184 Gln His Gln Ser Trp Leu Arg Pro Val Leu Arg Ser Asn Arg Val Glu
185          20          25          30
186 Tyr Cys Trp Cys Asn Ser Gly Arg Ala Gln Cys His Ser Val Pro Val
187          35          40          45
188 Lys Ser Cys Ser Glu Pro Arg Cys Phe Asn Gly Gly Thr Cys Gln Gln
189          50          55          60
190 Ala Leu Tyr Phe Ser Asp Phe Val Cys Gln Cys Pro Glu Gly Phe Ala
191 65          70          75          80
192 Gly Lys Cys Cys Glu Ile Asp Thr Arg Ala Thr Cys Tyr Glu Asp Gln
193          85          90          95
194 Gly Ile Ser Tyr Arg Gly Thr Trp Ser Thr Ala Glu Ser Gly Ala Glu
195          100          105          110
196 Cys Thr Asn Trp Asn Ser Ser Ala Leu Ala Gln Lys Pro Tyr Ser Gly
197          115          120          125
198 Arg Arg Pro Asp Ala Ile Arg Leu Gly Leu Gly Asn His Asn Tyr Cys
199          130          135          140
200 Arg Asn Pro Asp Arg Asp Ser Lys Pro Trp Cys Tyr Val Phe Lys Ala
201 145          150          155          160
202 Gly Lys Tyr Ser Ser Glu Phe Cys Ser Thr Pro Ala Cys Ser Glu Gly
203          165          170          175
204 Asn Ser Asp Cys Tyr Phe Gly Asn Gly Ser Ala Tyr Arg Gly Thr His
205          180          185          190
206 Ser Leu Thr Glu Ser Gly Ala Ser Cys Leu Pro Trp Asn Ser Met Ile
207          195          200          205
208 Leu Ile Gly Lys Val Tyr Thr Ala Gln Asn Pro Ser Ala Gln Ala Leu
209          210          215          220
210 Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Gly Asp Ala Lys

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TIME: 09:37:01

Input Set : A:\568.1D1.TXT

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```

211 225          230          235          240
212 Pro Trp Cys His Val Leu Lys Asn Arg Arg Leu Thr Trp Glu Tyr Cys
213          245          250          255
214 Asp Val Pro Ser Cys Ser Thr Cys Gly Leu Arg Gln Tyr Ser Gln Pro
215          260          265          270
216 Gln Phe Glu Ile Lys Gly Gly Leu Phe Ala Asp Ile Ala Ser His Pro
217          275          280          285
218 Trp Gln Ala Ala Ile Phe Ala Lys His Arg Arg Ser Pro Gly Glu Arg
219          290          295          300
220 Phe Leu Cys Gly Gly Ile Leu Ile Ser Ser Cys Trp Ile Leu Ser Ala
221 305          310          315          320
222 Ala His Cys Phe Gln Glu Arg Phe Pro Pro His His Leu Thr Val Ile
223          325          330          335
224 Leu Gly Arg Thr Tyr Arg Val Val Pro Gly Glu Glu Glu Gln Lys Phe
225          340          345          350
226 Glu Val Glu Lys Tyr Ile Val His Lys Glu Phe Asp Asp Asp Thr Tyr
227          355          360          365
228 Asp Asn Asp Ile Ala Leu Leu Gln Leu Lys Ser Asp Ser Ser Arg Cys
229          370          375          380
230 Ala Gln Glu Ser Ser Val Val Arg Thr Val Cys Leu Pro Pro Ala Asp
231 385          390          395          400
232 Leu Gln Leu Pro Asp Trp Thr Glu Cys Glu Leu Ser Gly Tyr Gly Lys
233          405          410          415
234 His Glu Ala Leu Ser Pro Phe Tyr Ser Glu Arg Leu Tyr Glu Ala His
235          420          425          430
236 Val Arg Leu Tyr Pro Ser Ser Arg Cys Thr Ser Gln His Leu Leu Asn
237          435          440          445
238 Arg Thr Val Thr Asp Asn Met Leu Cys Ala Gly Asp Thr Arg Ser Gly
239          450          455          460
240 Gly Pro Gln Ala Asn Leu His Asp Ala Cys Gln Gly Asp Ser Gly Gly
241 465          470          475          480
242 Pro Leu Val Cys Leu Asn Asp Gly Arg Met Thr Leu Val Gly Ile Ile
243          485          490          495
244 Ser Trp Gly Leu Gly Cys Gly Gln Lys Asp Val Pro Gly Val Tyr Thr
245          500          505          510
246 Lys Val Thr Asn Tyr Leu Asp Trp Ile Arg Asp Asn Met Arg Pro
247          515          520          525

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250 &lt;210&gt; SEQ ID NO: 4

251 &lt;211&gt; LENGTH: 290

252 &lt;212&gt; TYPE: DNA

253 &lt;213&gt; ORGANISM: Homo sapiens

255 &lt;400&gt; SEQUENCE: 4

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257 cagactgtac ccattccagcc gctgcacatc acaacattta cttaacagaa cagtcaccga 120
258 caacatgctg tgtgctggag acactcggag cggcggggccc caggcaaact tgcacgacgc 180
259 ctgccagggc gattcggggag gcccctgtgt gtgtctgaac gatggccgca tgacttttgt 240
260 gggcatcatc agctggggcc tgggctgtgg acagaaggat gtcccgggtg 290

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262 &lt;210&gt; SEQ ID NO: 5

263 &lt;211&gt; LENGTH: 290

VERIFICATION SUMMARY

DATE: 10/07/2004

PATENT APPLICATION: US/10/705,633A

TIME: 09:37:02

Input Set : A:\568.1D1.TXT

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